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10/549,289	08/14/2006	Tomoyuki Tahara	081356-0248	1968

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
OGUNBIYI, OLUWATOSIN A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,289	TAHARA ET AL.	
	Examiner	Art Unit	
	Oluwatosin Ogunbiyi	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,6-47,49,54,55,60,61,66 and 67* is/are pending in the application.

4a) Of the above claim(s) *49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,6-47,54,55,60,61,66 and 67* is/are rejected.

7)☒ Claim(s) *2,7,18,19,28,29,38,39,54 and 55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/16/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment to the claims filed 1/15/2008 is entered into the record. Claims 1, 3-5, 48, 50-53, 56-59, 62-65 are cancelled. Claims 2, 6-47, 49, 54-55, 60-61 and 66-67 are pending in the application. Claims 2, 6-47, 54-55, 60-61 and 66-67 are under examination.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Specification

The disclosure is objected to because of the following informalities: The brief description of Fig. 2 does not reflect the information contained in Fig. 2. It appears that said brief description for Fig. 2 might be for Fig. 3. Appropriate correction is required.

Applicants' assistance is requested in correcting any other typographical or grammatical errors that may be present in the specification.

Information Disclosure Statement

The information disclosure statement filed 9/16/05 has been considered. An initialed copy is enclosed.

Election/Restrictions

Applicant's election with traverse of Group 1 claims 1-47, 49,54,55,60 and 61 and species "activity of inhibiting the coaggregation of P. gingivalis and activity of promoting human neutrophilic phagocytosis" in the lack of unity mailed 10/18/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 49 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Objections

Claims 2,7,18,19,28,29,38,39,54 and 55 are objected to because of the following informalities: The instant claims contain the acronym OMP. While acronyms are permissible shorthand in the claims, the first recitation (i.e. in an independent claim) should include the full recitation followed by the acronym in parenthesis. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2,6,7,8,14,15,16,19, 23, 24,25, 29,30,33,34,35,39,43,44 and 45, are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

An antibody binding to a 40 kDa OMP or a functional fragment thereof can exist naturally in nature. For instance, a subject infected with *P. gingivalis* can naturally produce polyclonal antibodies to a 40 kDa OMP protein of said *P. gingivalis*. The recitation of *isolated* will reflect the hand of man in the antibody in the claims. In addition, as to claims 19, 29 and 39, polyclonal antibodies naturally produced in response 40 kDa OMP protein or *P. gingivalis* infection will contain a polyclonal antibody that comprises variable regions of an antibody that is produced by the respective hybridomas.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of the hybridomas with accession numbers FERM BP 8325, FERM BP 8323 and FERM BP 8324. Because it is not clear that the hybridomas with the properties of said accession numbers are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claim requires said hybridoma, a suitable deposit for patent purposes is required. Exact replication of the hybridoma is an unpredictable event.

Applicant's referral to the deposit of the hybridomas on p. 16 and 25 of the specification is an insufficient assurance that all required deposits have been made and all the conditions of 37 CFR §1.801-1.809 have been met.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, *that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.* This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance

may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;

2) The name and address of the depositor;

3) The date of deposit;

4) The identity of the deposit and the accession number given by the depository;

5) The date of the viability test;

6) The procedures used to obtain a sample if the test is not done by the depository; and

7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

Applicant's attention is directed *to In re Lundack*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Claims 54,55, 60,61,66 and 67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent that suppresses or treats alveolar bone resorption due to *P. gingivalis* which contains an antibody binding to a 40 kDa OMP does not reasonably provide enablement for an agent for preventing, diagnosing or treating periodontal diseases or for suppressing alveolar bone resorption caused by other microorganisms, which contains an antibody binding to a 40 kDa OMP. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to an agent for preventing, diagnosing, treating periodontal diseases or suppressing alveolar bone resorption, which contains an antibody or functional fragment thereof that binds to 40 kDa OMP or a functional fragment thereof.

The facts that should be considered in determining whether a specification is enabling or if it would require an undue amount of experimentation to practice the invention include 1) the quantity of experimentation necessary to make or use the invention based on the content of the disclosure, (2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988). The determination that "undue

experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, the factors that weigh more in making the instant enablement rejection are discussed below.

Breadth of the claims and the nature of the invention – the nature of the invention is drawn to an antibody that binds to a 40 kDa OMP that prevents diagnoses or treats periodontal diseases or suppresses alveolar bone resorption. Periodontal diseases includes dental plaque induced gingival diseases; non-plaque induced gingival lesions (of fungal, of viral, of bacterial (*Treponema, Neisseria* other bacteria) and of genetic origin, gingival manifestations of systemic conditions (mucocutaneous disorders, allergic reactions, traumatic lesions, foreign body reactions)); chronic periodonitis; aggressive periodonitis; periodonitis as a manifestation of a systemic disease (associated with hematological disorder, associated with genetic disorders); necrotizing periodontal diseases; abscesses of periodonitis; periodonitis associated with endodontic lesions and developmental or acquired deformities and conditions. See Armitage et al. Periodontology 2000, vol. 30, 2002, 9-23, p. 17). As to alveolar bone resorption, this condition is not only due to P. gingivalis but is also caused by other bacteria such as *Bacteriodes fortsythus, Actinobacillus actionomycetemcomitans* and *Prevotella intermedia* (Baker et al. Microbes and Infection, 2, 2000, p. 1181-1192 see p. 1183-1184). Therefore, the scope of the claims is broad as to periodontal diseases and alveolar bone resorption caused by any infectious microorganism.

The amount of direction or guidance presented; the presence or absence of working examples – The specification teaches that antibodies to 40 kDa OMP were administered to rats

and then said rats were challenged with *P. gingivalis*. Said rat had a reduced amount of alveolar bone resorption compared to rats not immunized with said antibody but challenged with *P. gingivalis* (see fig. 7 compare columns 3 and 4). However, alveolar bone resorption was not prevented but only reduced to levels of bone resorption in mice that are sham inoculated (i.e. not inoculated with antibodies and not challenged with P. *gingivalis* – compare columns 1 and 3 figure 7.

The specification does not provide any correlation between the passive immunity provided by said antibodies with prevention of alveolar bone resorption. The specification only provides evidence for suppression of alveolar resorption due to *P. gingivalis*. It appears that some alveolar bone resorption normally occurs in the rats used in the study as evidenced by its occurrence in non-immunized control rats wherein alveolar resorption has not been induced. Thus, based on the evidence the instant antibodies suppress alveolar bone resorption due to *P. gingivalis* but does not prevent alveolar bone resorption that occurs normally or due to other reasons such as other microorganisms. Furthermore, the specification does not provide any correlation between the passive immunity provided by said antibodies with prevention or treatment of other periodontal diseases. The scope of periodontal diseases is very broad as set forth above. See p. 17 of Armitage et al for a listing of different types of periodontal diseases.

For example, the specification does not provide any correlation between the passive immunity provided by said antibodies with prevention of periodontal diseases of genetic origin or periodontal diseases caused by viruses, fungi, other bacteria such as *Neisseria, Treponema*. The specification does not correlate passive immunity afforded by said antibodies with broad protection against or for treatment of all periodontal diseases. Also, the specification does not teach how to use the instant antibody to diagnose all these periodontal diseases.

The state of the art and the unpredictability of the art – The art teaches that a monoclonal antibody raised against a 40 kDa OMP did not recognize other periodontal disease associated bacteria and that the bactericidal activity of said antibody is specific for *P. gingivalis* (Katoh et al. J. Periodontol. 2000; 71:368-375, p. 369 under preparation of Pg-ompA2). Thus, it is unpredictable whether the instantly claimed antibody will be bactericidal against virus, fungi and other bacteria that cause some types of periodontal disease or periodontal diseases that are non-pathogen related. Further, the art teaches that monoclonal antibodies to *P. gingivalis* have been used to study the *role* of *P. gingivalis* in periodontal disease (Booth et al. 1996, Infection and Immunity p. 422-27) but the art is silent as to how to use said antibodies to diagnose any periodontal disease. Thus, it unpredictable as to whether the instant antibodies can diagnose periodontal diseases.

In view of the above factors it would require undue experimentation on the part of the skilled artisan to use the invention as claimed to prevent, treat or diagnose periodontal disease; and to use the invention to suppress alveolar bone resorption caused by other infectious microorganisms apart from *P. gingivalis*.

Claims 2, 6-47, 54-55,60-61 and 66-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to an antibody binding to 40-kDa OMP or functional fragment thereof, which has activity of inhibiting the coaggregation of P. gingivalis and (2) of promoting human neutrophilic phagocytosis.

It is not clear in the claims which functional fragment thereof is being referred to. Is it the functional fragment of the antibody or the functional fragment of the 40 kDa OMP?

In addition, as to claims 11-13, 20-22,30-32 and 40-42, how can the antibody bind a 40 kDa OMP protein and also bind to a therapeutic agent? Do Applicants' mean to say that the therapeutic agent is conjugated to the antibody as disclosed on p. 19 of the specification?

As to claims 25, 35, and 45 the claim is confusing because how can an antibody with an IgG variable region produced by hybridoma h13-17 or produced by hybridoma 5-89-2 or produced by hybridoma a44-1 also be an antibody of class IgA. The instant specification teaches that the antibodies produced by these hybridomas are of the class IgG (see p.31 table 1).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 6, 7, 9, 10, 14,15, 54,55,60 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997.

The claims are drawn to an antibody binding to 40-kDa OMP, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis.

Saito et al teaches an antibody binding to 40 kDa OMP. Said antibody has activity of inhibiting coaggregation of *P. gingivalis* and *Actinomyces viscosus* (See abstract). Since the instant claims do not distinguish the structure of the instantly claimed antibody from that of the prior art, said antibody binding to 40 kDa OMP will inherently have activity of promoting human neutrophilic phagocytosis; and inherently have activity of suppressing alveolar bone resorption. Said antibody is produced by a mouse-mouse hybridoma (see p. 675 under monoclonal antibodies and hybridoma cells isolated from mice immunized with recombinant 40 kDa OMP); said antibody is a monoclonal antibody (p. 675 monoclonal antibodies). Saito et al teaches said antibody of class IgG wherein IgG is IgG1 (see page 677 first paragraph under results). The instant claims are drawn to the products i.e. the antibody and not to a method of using said products. Thus, Saito et al anticipates the antibody set forth in claims 54,55;60 and 61, as set forth above.

Claims 2, 6, 7, 8, 10,14,15, 54, 55,60 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969.

The claims are drawn to an antibody binding to 40-kDa OMP thereof, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis.

Abiko et al teaches an antibody binding to 40 kDa OMP. Said antibody has activity of inhibiting coaggregation of *P. gingivalis* and *Actinomyces viscosus* (See p. 3966 – abstract, right column which teaches that *Actinomyces viscosus* is now included in *Actinomyces naeslundii* and p. 3967 fig. 2). Since the instant claims do not distinguish the structure of the instantly claimed antibody from that of the prior art, said antibody binding to 40 kDa OMP will inherently have activity of promoting human neutrophilic phagocytosis; and inherently have activity of suppressing alveolar bone resorption. Said antibody is a human antibody; said antibody is a monoclonal antibody (see whole article). Abiko et al teaches said antibody of class IgG wherein IgG is IgG1 (see page 3967 bottom of first incomplete paragraph). The instant claims are drawn to the products i.e. the antibody and not to a method of using said products. Thus, Abiko et al anticipates the antibody set forth in claims 54,55,60,61 and 66-67 as set forth above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 6, 7, 9, 10, 14,15, 54,55,60 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997 view of Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 and 477.

The claims are drawn to a functional fragment of an antibody binding to 40-kDa OMP, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis.

Saito et al teaches an antibody binding to 40 kDa OMP. Said antibody has activity of inhibiting coaggregation of *P. gingivalis* and *Actinomyces viscosus* (See abstract). Since the instant claims do not distinguish the structure of the instantly claimed antibody from that of the prior art, said antibody binding to 40 kDa OMP will inherently have activity of promoting human neutrophilic phagocytosis; and inherently have activity of suppressing alveolar bone resorption. Said antibody is produced by a mouse-mouse hybridoma (see p. 675 under monoclonal antibodies and hybridoma cells isolated from mice immunized with recombinant 40 kDa OMP); said antibody is a monoclonal antibody (p. 675 monoclonal antibodies). Saito et al teaches said antibody of class IgG wherein IgG is IgG1 (see page 677 first paragraph under results). The

instant claims are drawn to the products i.e. the antibody and not to a method of using said products. Thus, Saito et al anticipates the antibody set forth in claims 54,55,60 and 61, as set forth above.

Saito et al does not teach functional fragment of said antibody

Abbas et al teaches proteolytic fragments of an immunoglobulin G molecule obtained by papain and pepsin digestion. Abbas et al teaches that papain digestion results in the Fc fragment which binds to Fc receptors and activates complement and pepsin digestion generates a single bivalent antigen binding fragment with higher avidity for antigen (p. 55). Abbas et al teaches that Fc fragments activate complement while Fab fragments are used in research and therapeutic applications when antigen binding is desired without activation of effector functions p. 477).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to obtain pepsin or papain fragments of the antibody of Saito et al as taught by Abbas et al because Abbas et al teaches that papain digestion results in the Fc fragment which binds to Fc receptors and activates complement and pepsin digestion generates a single bivalent antigen binding fragment (Fab fragment). One of skill in the art would be motivated to make such fragments because Abbas et al teaches that Fc fragments activate complement while Fab fragments are used in research and therapeutic applications when antigen binding is desired without activation of effector functions.

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997 and Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 and 477 as applied to claims 2, 6, 7, 9, 10, 14,15,

54,55,60 and 61 above further in view of Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004.

The claims are drawn to an antibody binding to 40-kDa OMP or functional fragment thereof , which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis, which covalently binds to a therapeutic agent wherein the antibody thereof binds to a antibiotic or antibacterial agent.

The combination of Saito and Abbas is set forth supra. Said combination does not teach that said antibody or functional fragment thereof covalently bound to therapeutic agents such as antibiotics or antibacterial.

Carroll et al teach antibody-antibiotic conjugates. Carroll et al teach that antibodies have many reactive groups that can be used in covalent conjugation to antibodies and teaches fragments of antibodies to make antibody-antibiotic conjugates (fig. 1B, column 11, column 14 lines 59-64, column 15 lines 46-50. Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing (column 9 lines 15-23).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to bind or link an antibiotic or antibacterial covalently to the antibody or functional fragment thereof of Saito et al and Abbas et al as combined as taught by Carroll et al because Carroll et al teach antibodies and functional fragments have many reactive groups that can be used in covalent conjugation to antibodies and because Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over

Saito et al. Gen. Pharmac. Vol. 28, p. 675-680, 1997 and Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 and p. 477 and Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004 as applied to claims 2, 6, 7, 9-12 14,15, 54,55,60 and 61 further in view of Alakhov et al. US 5,840,319, 1998.

The claims are drawn to an antibody or functional fragment binding to 40-kDa OMP , which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis, which covalently or non-covalently binds to a therapeutic agent wherein the antibody thereof binds to a antibiotic or antibacterial agent such as tetracycline or minocycline.

The combination of Saito and Abbas and Carroll is set forth supra. Said combination does not teach non-covalent binding of therapeutic agents to an antibody or functional fragment thereof and does not teach therapeutic agents such as tetracycline or minocycline.

Alakhov teaches antibiotic or antibacterial therapeutic agents such as tetracycline or minocycline that are non-covalently bound to an antibody (column 2 lines 59-61, column 3 and 4 definition of chemotherapeutic agent and targeting moiety, column 12 lines 28-30 and lines 48-51 and column 15 lines16-18).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to use another means known in the art for binding the therapeutic agent/antibiotic agent/antibacterial agent to the antibody or functional fragment thereof Saito and Abbas and Carroll as combined such as non-covalent binding taught by Alakhov et al because Alakhov teaches such a means by which an antibiotic or antibacterial therapeutic agent is non-covalently bound to an antibody and one of skill in the art would be motivated to make such a conjugate of an antibody or functional fragment thereof with an

antibacterial/antibiotic because Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing. Further, Alakhov teaches antibiotics/antibacterial such as tetracycline or minocycline that can be used to make such conjugates.

Claims 2, 6, 7, 8, 10,14,15, 54, 55,60 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 view of Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55.

The claims are drawn to a functional fragment of an antibody binding to 40-kDa OMP, which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis.

Abiko et al teaches an antibody binding to 40 kDa OMP. Said antibody has activity of inhibiting coaggregation of *P. gingivalis* and *Actinomyces viscosus* (See p. 3966 – abstract, right column which teaches that *Actinomyces viscosus* is now included in *Actinomyces naeslundii* and p. 3967 fig. 2). Since the instant claims do not distinguish the structure of the instantly claimed antibody from that of the prior art, said antibody binding to 40 kDa OMP will inherently have activity of promoting human neutrophilic phagocytosis; and inherently have activity of suppressing alveolar bone resorption. Said antibody is a human antibody; said antibody is a monoclonal antibody (see whole article). Abiko et al teaches said antibody of class IgG wherein IgG is IgG1 (see page 3967 bottom of first incomplete paragraph). The instant claims are drawn to the products i.e. the antibody and not to a method of using said products. Thus, Abiko et al anticipates the antibody set forth in claims 54,55,60,61 and 66-67 as set forth above.

Abiko et al does not teach a functional fragment of said antibody

Abbas et al teaches proteolytic fragments of an immunoglobulin G molecule obtained by papain and pepsin digestion. Abbas et al teaches that papain digestion results in the Fc fragment which binds to Fc receptors and activates complement and pepsin digestion generates a single bivalent antigen binding fragment with higher avidity for antigen (p. 55). Abbas et al teaches that Fc fragments activate complement while Fab fragments are used in research and therapeutic applications when antigen binding is desired without activation of effector functions p. 477).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to obtain pepsin or papain fragments of the antibody of Abiko et al as taught by Abbas et al because Abbas et al teaches that papain digestion results in the Fc fragment which binds to Fc receptors and activate complement and pepsin digestion generates a single bivalent antigen binding fragment with higher avidity for antigen. One of skill in the art would be motivated to make such fragments because Abbas et al teaches that Fc fragments activate complement while Fab fragments are used in research and therapeutic applications when antigen binding is desired without activation of effector functions.

Claims 11-12, are rejected under 35 U.S.C. 103(a) as being unpatentable over Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 and Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 as applied to claims 2, 6, 7, 8, 10,14,15, 54, 55,60 and 61 above further in view of Carroll et al US 6,660,267, Dec. 9, 2003 filed 9/12/2004.

The claims are drawn to an antibody binding to 40-kDa OMP or functional fragment thereof , which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting

human neutrophilic phagocytosis, which covalently binds to a therapeutic agent wherein the antibody thereof binds to a antibiotic or antibacterial agent.

The combination of Abiko and Abbas is set forth supra. Said combination does not teach that said antibody or functional fragment thereof covalently bound to therapeutic agents such as antibiotics or antibacterial.

Carroll et al teach antibody-antibiotic conjugates. Carroll et al teach that antibodies have many reactive groups that can be used in covalent conjugation to antibodies and teaches fragments of antibodies to make antibody-antibiotic conjugates (fig. 1B, column 11, column 14 lines 59-64, column 15 lines 46-50. Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing (column 9 lines 15-23).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to bind or link an antibiotic or antibacterial covalently to the antibody or functional fragment thereof of Abiko et al and Abbas et al as combined as taught by Carroll et al because Carroll et al teach antibodies and functional fragments have many reactive groups that can be used in covalent conjugation to antibodies and because Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Abiko et al. Infection and Immunity, Sept. 1997, p. 3966-3969 and Abbas et al. Cellular and Molecular Immunology 4th edition, 2000, p. 55 and Carroll et al US 6,660,267, Dec. 9, 2003 filed

9/12/2004 as applied to claims 2, 6, 7, 8, 10-12,14,15, 54, 55,60 and 61 further in view of Alakhov et al. US 5,840,319, 1998.

The claims are drawn to an antibody or functional fragment binding to 40-kDa OMP , which has activity of inhibiting the coaggregation of *P. gingivalis* and (2) of promoting human neutrophilic phagocytosis, which covalently or non-covalently binds to a therapeutic agent wherein the antibody thereof binds to a antibiotic or antibacterial agent such as tetracycline or minocycline.

The combination of Abiko and Abbas and Carroll is set forth supra. Said combination does not teach non-covalent binding of therapeutic agents to an antibody or functional fragment thereof and does not teach therapeutic agents such as tetracycline or minocycline.

Alakhov teaches antibiotic or antibacterial therapeutic agents such as tetracycline or minocycline that are non-covalently bound to an antibody (column 2 lines 59-61, column 3 and 4 definition of chemotherapeutic agent and targeting moiety, column 12 lines 28-30 and lines 48-51 and column 15 lines16-18).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to use another means known in the art for binding the therapeutic agent/antibiotic agent/antibacterial agent to the antibody or functional fragment thereof of Abiko and Abbas and Carroll as combined such as non-covalent binding taught by Alakhov et al because Alakhov teaches such a means by which an antibiotic or antibacterial therapeutic agent is non-covalently bound to an antibody and one of skill in the art would be motivated to make such a conjugate of an antibody or functional fragment thereof with an antibacterial/antibiotic because Carroll et al teach that said conjugates provide the advantage of binding and opsonization of bacteria and direct bacterial killing. Further, Alakhov teaches

antibiotics/antibacterial such as tetracycline or minocycline that can be used to make such conjugates.

Status of the Claims

Claims 2, 6-47, 54-55, 60-61 and 66-67 are rejected. Claims 2,7,18,19,28,,29,38,39,54 and 55 are objected to. No claims allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Examiner Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Oluwatosin Ogunbiyi

Examiner

Art Unit 1645

PATRICIA A. DUFFY
PRIMARY EXAMINER